II.

Agency finds that, both independently and cumulatively, the evidence of foreseeable pharmacological effects and uses, actual consumer use for pharmacological purposes, and manufacturer intent as revealed through the statements, research, and actions of the manufacturers convincingly supports the Agency's determination that cigarettes and smokeless tobacco are intended to affect the structure and function of the body.

A. A REASONABLE MANUFACTURER WOULD FORESEE THAT CIGARETTES AND SMOKELESS TOBACCO WILL CAUSE ADDICTION AND OTHER PHARMACOLOGICAL EFFECTS AND WILL BE USED BY CONSUMERS FOR PHARMACOLOGICAL PURPOSES

FDA may conclude that a product is intended to affect the structure or function of the body if a reasonable person in the position of the manufacturer would foresee that the product will have pharmacological effects and that a substantial proportion of consumers will use the product for those effects. In the Jurisdictional Analysis, the Agency made extensive findings, based on the evidence then available, regarding the pharmacological effects of tobacco on the human body. *See* Jurisdictional Analysis, 60 FR 41534–41575. FDA received comments on these findings from the tobacco industry, many medical and public health organizations and medical practitioners, and from other members of the public. The administrative record includes extensive, publicly disseminated evidence from scientific studies and expert panels on the subject of tobacco's pharmacological effects on the human body.

After considering the administrative record and reviewing public comments, the Agency finds that the evidence clearly demonstrates that a reasonable tobacco manufacturer would foresee that cigarettes and smokeless tobacco will cause and sustain addiction, produce other psychoactive effects, and control weight and be used by consumers for these effects. This finding provides an independent basis for the Agency's conclusion that cigarettes and smokeless tobacco are intended to affect the structure and function of the body.

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In section II.A.1., below, FDA describes the legal basis for considering evidence of the foreseeable effects and uses of a product. FDA presents its major findings and responds to significant comments in sections II.A.2. through II.A.6. In section II.A.7., FDA responds to the remaining relevant substantive comments.

1. "Intended Use" May Be Established on the Basis of Foreseeable Pharmacological Effects and Uses

The Agency's legal authority to establish intended use based on the foreseeable effects and the foreseeable uses of a product comes from the plain language of the Act, as well as from FDA's regulations, case law, administrative precedent, and the public health purposes of the Act.

The plain language of the Act provides that a drug or device is an article "*intended* to affect the structure or any function of the body." Sections 201(g)(1)(c) and 201(h)(3) of the Act, 21 U.S.C. 321(g)(1)(C), 321(h)(3) (emphasis added). It is a widely accepted legal principle that persons can be held to "intend" the reasonably foreseeable consequences of their actions. In 1938, when Congress defined drugs and devices as articles "intended" to affect the structure or any function of the body of man, it was well established that "[t]he law presumes that every man *intends* the legitimate consequences of his own acts." *Agnew v. United States*, 165 U.S. 36, 53 (1897); *accord Fanning v. United States*, 72 F.2d 929, 932 (4th Cir. 1934) ("the law imputes an intent to accomplish the natural results of one's own act") (citations omitted); *Eastern Drug Co. v. Bieringer-Hanauer Co.*, 8 F.2d 838, 839 (1st Cir. 1925) ("presumption that one intends the natural and probable consequences of his acts"); *see also* 4 *Wigmore on Evidence* 3388-3390

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(1904-1905) (intent is "a volition having consequences which ought reasonably to have been foreseen"), *quoted in Rushmore v. Saxon,* 158 F. 499, 506 (C.C.S.D.N.Y. 1908).

In accordance with this well-accepted legal principle, FDA may establish that a manufacturer "intends" that its product affect the structure or function of the body when it is foreseeable that the product will in fact affect the structure or function of the body in a drug-like manner. The case for establishing intent through foreseeability is especially strong when a reasonable manufacturer would foresee that a product will *both* act like a drug *and* be commonly used like a drug. Where it is foreseeable that a product will have pharmacological effects on a significant proportion of consumers and will be used by these consumers to obtain these pharmacological effects, the statute allows FDA to recognize reality and find that the manufacturer "intends" its product to be used as a drug.

Consistent with this well-established understanding of "intent," FDA's regulations defining "intended use" contemplate that foreseeability can be a basis for establishing the objective intent of the manufacturer. These regulations require product labeling to include adequate directions for all "intended uses." 21 CFR 201.5 (drugs); 21 CFR 801.5 (devices). The intended uses of a drug or device that must be included on the label are defined to include those that are, or that reasonably can be, anticipated by the manufacturer.

The definition of "intended uses" for drugs establishes an "objective intent" standard. Specifically, the regulations provides:

> The words "intended use" or words of similar import . . . refer to the objective intent of the persons legally responsible for the labeling of drugs. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example,

> be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives. It may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. The intended uses of an article may change after it has been introduced into interstate commerce by its manufacturer. If, for example, a packer, distributor, or seller intends an article for different uses than those intended by the person from whom he received the drug, such packer, distributor, or seller is required to supply adequate labeling in accordance with the new intended uses. But *if a manufacturer knows, or has knowledge of facts that would give him notice, that a drug introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it,* he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put.

21 CFR 201.128 (emphasis added). The definition of "intended uses" for devices is essentially identical. 21 CFR 801.4. Thus, under these regulatory provisions, objective intent can be established by evidence showing that the manufacturer "knows" or "has knowledge of facts that would give him notice," i.e., that a reasonable manufacturer would foresee that consumers will use a product for drug or device uses.[23]

Other parts of the regulations also provide that foreseeable pharmacological uses should be considered to be intended by the manufacturer. Section 201.128, for instance,

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[23] The Agency disagrees with the tobacco industry's suggestion that this foreseeability test must be interpreted to apply only to products that are already classified as "drugs" or "devices." The Agency regularly uses the regulatory definition of "intended uses" to determine whether products should be classified as drugs or devices. *See, e.g., United States v. Articles of Drug*, 625 F.2d 665, 668 n.5 (5th Cir. 1980); *United States v. Undetermined Quantities of An Article or Drug Labeled as "Exachol,"* 716 F. Supp. 787, 791 (S.D.N.Y. 1989); *United States v. 22 . . . devices . . . "The Ster-o-lizer MD-200,"* 714 F. Supp. 1159, 1165 (D. Utah 1989); *United States v. Kasz Enterprises*, 855 F. Supp. 534, 539 (D.R.I. 1994), modified on other grounds, 862 F. Supp. 717 (D.R.I. 1994); *United States v. Articles of Food and Drug Consisting of . . . Apricots*, 444 F. Supp. 266, 273 (E.D. Wis. 1977). Thus, the Agency relies on the test of objective intent in the regulation (including the foreseeability standard described above) to establish: (1) in the case of products already classified as drugs or devices, the intended uses that must appear on the product labeling; and (2) in the case of products not yet classified as drugs or devices, the intended uses that determine whether the product should be classified as a drug or device. The Agency's interpretation of its own regulation is reasonable and entitled to "controlling weight." *Thomas Jefferson Univ.* 114 S. Ct. 2381, 2386 (1994).

further provides that "objective intent . . . may be shown by the circumstance that the article is, *with the knowledge of such persons* or their representatives, *offered and used for a purpose for which it is neither labeled nor advertised.*"[24] 21 CFR 201.128 (emphasis added).

The case law and administrative precedent interpreting the Act recognize that the foreseeable pharmacological effects and uses of a product are proper grounds for establishing intent. These precedents recognize that the Agency may consider evidence of the likely consumer use of a product in determining intended use. *See, e.g., Two Plastic Drums*, 761 F. Supp. at 72; *Kasz*, 855 F. Supp. at 539. They also recognize that a foreseeable drug effect is generally persuasive evidence that the product is intended to affect the structure and function of the body. For example, the court in *United States v. Undetermined Quantities . . . "Pets Smellfree"* found that the presence of chlortetracycline, a drug ingredient, at doses sufficient to reduce the level of bacteria in animal intestines was evidence that the product was intended to affect the structure and function of the body. 22 F.3d 235, 240 (10th Cir. 1994).[25] Indeed, the court found this evidence to be relevent even though the dose of chlortetracycline in the product was "subtherapeutic"—that is, the dose was sufficient to reduce bacteria levels, but not to cure

[24] The tobacco industry contends that the requirement that the product must be "offered" as well as used for an unlabeled or unadvertised use means that there must be a specific marketing representation promoting the use. The Agency does not so interpret the regulation. The ordinary definition of the word "offer" means simply "[t]o present for acceptance or rejection." *American Heritage Dictionary of the English Language* (3d ed. 1992) at 1255. Moreover, the tobacco industry's interpretation conflicts with the language in the regulation that provides that the use for which the product is offered is a use "for which it is neither labeled nor advertised." Consistent with the language of the regulation, the Agency interprets the requirement that the product be "offered" to mean simply that the product be presented to the consumer for purchase.

[25] *See* section II.E., below, for an additional discussion of the relevant case law and administrative precedent.

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or treat a disease. *Id.* Administratively, the Agency has asserted jurisdiction over products such as khat, imitation cocaine, hormone-containing skin creams, and fluoride-containing toothpastes based primarily, if not exclusively, on evidence that these products have foreseeable drug effects and drug uses. *See* section II.E.1.e., below.

Cases interpreting other public health statutes establish a test for determining intended use that is the same as the one used by FDA and that permits reliance on foreseeable uses. In *N. Jonas & Co. v. EPA*, 666 F.2d 829 (3d Cir. 1981), for example, the court held that a product was "intended for use" as a pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) based on its foreseeable consumer use—even though the manufacturer did not promote the product as a pesticide (and even disclaimed use as a pesticide on the label). The court stated:

> The Act [and] the regulations . . . focus inquiry on the intended use, implicit or expressed. *We take this to mean the use which a reasonable consumer would undertake . . . . In determining intent objectively, the inquiry cannot be restricted to a product's label and to the producer's representations. Industry claims and general public knowledge can make a product pesticidal notwithstanding the lack of express pesticidal claims by the producer itself.*

Id. at 833 (emphasis added).

Similarly, in *United States v. Focht*, 882 F.2d 55, 60 (3d Cir. 1989), the court held that under the Federal Hazardous Substances Act (FHSA), "[i]ntended use . . . , objectively defined, necessarily encompasses foreseeability." In this case, the Consumer Product Safety Commission sought to take action against fireworks components that could be assembled to make banned fireworks. The court found that the testimony that 90% of consumers who order the components will use the components to make illegal fireworks "makes it foreseeable that the components in question will be used to build

banned fireworks. Such knowledge must be attributed to [the defendants]." *Id.; accord United States v. Articles of Banned Hazardous Substances . . . Baby Rattles,* 614 F. Supp. 226 (E.D.N.Y. 1985).

The tobacco industry argues that the Agency may not rely on the interpretation of "intended use" in other statutes to interpret "intended use" under the Federal Food, Drug, and Cosmetic Act. The fact that FDA's interpretation of "intended use" under the Federal Food, Drug, and Cosmetic Act parallels the interpretation under other public health statutes, however, strongly supports the reasonableness of the Agency's analysis. Indeed, the court in *Jonas* relied in part on cases interpreting intended use under the Federal Food, Drug, and Cosmetic Act in holding that intended uses encompass readily foreseeable consumer uses, specifically citing *National Nutritional Foods Ass'n (NNFA) v. Mathews,* 557 F.2d 325, 334 (2d Cir. 1977), for the proposition that "FDA [is] not bound by manufacturer's subjective claims of intent in assessing whether product is intended as a drug," and *Bacto-Unidisk,* 394 U.S. 784 (1969), for the proposition that "the definition of drug [is] to be given liberal interpretation in light of remedial purpose of Federal Food, Drug and Cosmetic Act." 666 F.2d at 833.[26]

Moreover, contrary to the tobacco industry's contention, the FHSA and FIFRA cannot be distinguished from the Federal Food, Drug, and Cosmetic Act on the ground that foreseeability principles are alien to the Federal Food, Drug, and Cosmetic Act. Several other provisions of the Act contemplate foreseeability principles. *See, e.g.,* 21

[26] Similarly, courts interpreting the Federal Food, Drug, and Cosmetic Act rely on interpretations of analogous consumer protection statutes. *See, e.g., "Sudden Change,"* 409 F.2d 734, 741 n.8 (2d Cir. 1969) (citing a case interpreting the Federal Trade Commission Act because "the remedial purpose of the Federal Trade Commission Act is sufficiently analogous").

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U.S.C. 321(n) (an article may be misbranded if its labeling and advertising fail to reveal "consequences which may result from . . . such conditions of use as are customary or usual"); 21 U.S.C. 360h (FDA authorized to recall devices that "present[] an unreasonable risk of substantial harm").

Indeed, in *United States v. Park*, 421 U.S. 658 (1975), the Supreme Court concluded that the Federal Food, Drug, and Cosmetic Act imposes "requirements of foresight and vigilance" on manufacturers, stating:

> the Act imposes not only a positive duty to seek out and remedy violations when they occur but also, and primarily, a duty to implement measures that will insure that violations will not occur. The requirements of *foresight and vigilance* imposed on responsible corporate officials are beyond question demanding, and perhaps onerous, but they are no more stringent than the public has a right to expect of those who voluntarily assume positions of authority in business enterprises whose services and products affect the health and well-being of the public that supports them.

Id. at 672 (emphasis added).

Compelling policy reasons support the Agency's interpretation that it may establish that a product is intended to affect the structure or function of the body when it is foreseeable that a product will produce significant pharmacological effects in consumers and be widely used by consumers for these effects. The manufacturers' position is that they may ignore overwhelming scientific evidence that their product will have and be used for pharmacological effects so long as they avoid promoting their product for these pharmacological effects. Under this interpretation, however, the manufacturer of virtually any drug or device could avoid regulation under the Act—no matter how substantial and well-established the pharmacological effects and uses of the product—by simply avoiding making certain claims in the product's labeling and advertising. For example, it is not

difficult to imagine a manufacturer of a generic version of a drug like Prozac (fluoxetine hydrochloride), an antidepressant drug currently available only by prescription, seeking to avoid FDA regulation by advertising its product as intended solely for the "pleasure" of its consumers. *See* section II.F.1.e., below.

Accepting the manufacturers' position would leave the public vulnerable to the unregulated distribution of products with known pharmacologically active ingredients. Moreover, it would reward manufacturers who deny the obvious pharmacological effects and uses of their products in their public statements, labeling, and advertising. Thus, the Agency concludes that the public health objectives of the Act require the Agency to regulate as "drugs" or "devices" products that can be foreseen to have widespread pharmacological effects and uses.

2. The Significant Pharmacological Effects and Uses of Cigarettes and Smokeless Tobacco Are Foreseeable

The evidence in the administrative record establishes that the pharmacological effects and uses of cigarettes and smokeless tobacco are so widespread and well-known that a reasonable manufacturer would foresee them. Since the Agency last considered the issue of whether cigarettes are drugs over 15 years ago, a scientific consensus has emerged that nicotine is addictive and has other significant pharmacological effects.

Nicotine—the essential ingredient in cigarettes and smokeless tobacco—is a pharmacological agent that substantially alters the structure and function of the brain and other systems of the body. After a single puff inhaled from a cigarette, nicotine enters the mouth, passes into the lungs, is absorbed from the lungs into the bloodstream, and diffuses